substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen; and

$R^{18'}$ is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

A17 cont.

$R^{20'}$ is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen;

$R^{21'}$ is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heterocyclic and substituted heterocyclic;

b is 1 or 2;

B is a nitrogen containing heteroaryl group;

and enantiomers, diastereomers and pharmaceutically acceptable salts thereof.

REMARKS

It is respectfully requested that the above amendments be entered and that this application be considered in view of these amendments and the following remarks.

Amendments

In the specification

The specification has been amended in Paragraphs 13-17, 27, 32, 34, 42, 47, 51, 58, 72, 159 and 167 to correct obvious typographical errors and to remove references to the variable "g" which is not present in any of the formulas herein. As such no new matter has been added.

In the Claims

Claim 3 and 4 have been amended to correct obvious typographical errors. As such no new matter has been added.

These amendments have been made in accordance with 37 C.F.R. §1.121 as amended on November 7, 2000. As required, attached hereto is an appendix illustrating the changes made to the Specification and the Claims.

Entry of these amendments is earnestly solicited.

Restriction Requirement

Claims 1-8 stand restricted into the following five groups defined in the Office Action as:

Group I: Claims 1 and 4, drawn to a compounds of formula I, classified in class 514, subclass 1+.

Group II: Claims 2 and 3, drawn to the compounds of formula II , classified in class 514, subclass 1+.

Group III: Claim 5, drawn to a pharmaceutical composition comprising a compound of formula I or formula II, classified in class 514, subclass 1+.

Group IV: Claim 6, drawn to a method for binding VLA-4 in a biological sample employing a compound of structural formula I or formula II, classified in class 514, subclass 1+.

Group V: Claims 7 and 8, drawn to a method for treating an inflammatory condition in a mammalian patient employing a compound of structural formula I or formula II, classified in class 514, subclass 1+.

In response to this restriction requirement, Applicants elect the invention defined by Group I drawn to a compounds of formula I, classified in class 514, subclass 1+, with traverse.

This restriction requirement is traversed because it is maintained that the five groups defined in the Office Action are drawn to sufficiently interrelated inventions to warrant examination thereof in a single application. Indeed, the compounds of Group I and Group II are classified in the same class (and subgroup) and contain overlapping compounds. For example, Formula I and Formula II converge upon the same compounds when, in Formula I, r=0, Alk^1 is not present, L^1 is OC(O)-N(R^{11})-, Ar is aryl or heteroaryl, and R^1, R^2 and R^3 are hydrogen, and, in Formula II, R^1 or R^2 is aryl or heteroaryl and the other of R^1 or R^2 is hydrogen, alkyl or substituted alkyl. In addition the pharmaceutical compositions of Group III and the methods of Group IV and V are substantially related to the Groups I and II compounds. Thus, a complete search of any of the defined Groups I-V would necessarily turn up art relevant with regard to the other groups. Accordingly, such a requirement for restriction is improper because it is inconsistent with the Patent Office's stated guidelines that an Examiner must examine the entire application on the merits if a search and examination can be conducted without serious burden. Specfically, MPEP § 803 states, in part, that "[I]f a search and examination of an entire application can be made without serious burden, the Examiner must examine the application on the merits, even though it includes claims to independent or distinct inventions." *MPEP § 803* at 800-3.

Applicants submit that Groups I and II at the very least can be searched simultaneously, and that a duplicative search, with possibly inconsistent results, may occur if the restriction requirement is maintained. If these groups are combined, the restriction should be cast as follows:

Group A: Claims 1-4, drawn to a compounds of formula I and formula II, classified in class 514, subclass 1+.

Group B: Claim 5, drawn to a pharmaceutical composition comprising a compound of formula I or formula II, classified in class 514, subclass 1+.

Group C: Claim 6, drawn to a method for binding VLA-4 in a biological sample employing a compound of structural formula I or formula II, classified in class 514, subclass 1+.

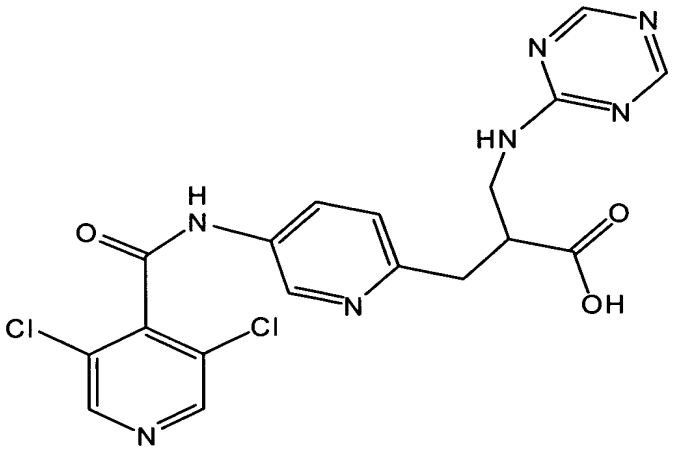
Group D: Claims 7 and 8, drawn to a method for treating an inflammatory condition in a mammalian patient employing a compound of structural formula I or formula II, classified in class 514, subclass 1+.

As maintained above, a complete search for all of the Groups would necessarily be coextensive such that search and examination of the entire application can be made without serious burden on the U.S. Patent and Trademark Office. Therefore, withdrawal of this restriction requirement is respectfully requested.

Election of Species

In addition to the above, the Office Action recites that Applicants are further required to elect a single, specific species for the elected group and a single disease or condition to be treated in Group IV-V, for examination purposes. See, for example, paragraph 1, page 5, of the Office Action.

Responsive to this election of species requirement, Applicants elect, without traverse the compound of formula I wherein R^1 is Cl (see page 12, paragraph [0039], line 2), R^2 is Cl (see page 12, paragraph [0039], line 2), R^3 is H (see page 12, paragraph [0039], line 2), Ar^1 is pyridyl (see page 14, paragraph [0041], line 5), r is 0 and alk^1 is absent (see page 10, paragraph [0030], line 1), L^1 is -C(O)NH- (see page 11, paragraph [0034], line 5), B is pyridylene (see page 48, paragraph [00136], line 3), R^4 and R^5 are H (see page 12, paragraph [0039], line 2), m is 1 and Alk^2 is $-CH_2-$ (see page 11, paragraph [0033], line 2), R is -C(O)OH (see page 5, paragraph [0013], line 21), R^6 is H (see page 23, paragraph [0069], line 1-2), R^a is H (see page 23, paragraph [0069], line 1-2), Ar^2 is 1,3,5-triazinyl (see page 23, paragraph [0070], line 7).



S-3-[3-(3,5-dichloropyrid-4-ylcarboamido)pyrid-6-yl]-2-(1,3,5-triazinylamino-methyl)propionic acid, for the treatment of asthma.

Applicant's believe that Claims 1, and 5-8 read on the elected species.

Early examination is requested.

Respectfully submitted,
BURNS, DOANE, SWECKER & MATHIS, L.L.P.

Date: January 31, 2003

By: _____
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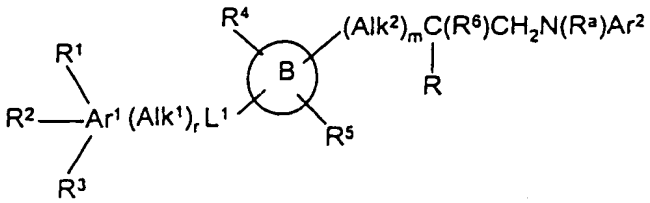
Attachment to the Reply and Amendment

Marked-up Copy

In the Specification

The chemical formula between paragraphs **[0012]** and **[0013]**.

[4]



(1)

Paragraph **[0013]** starting on Page 4:

[0013] wherein

Ar^1 is an aromatic or heteroaromatic group;

R^1, R^2, R^3, R^4 and R^5 which may be the same or different is each an atom or group $-L^2(Alk^3)_tL^3(R^7)_u$ in which L^2 and L^3 which may be the same or different is each a covalent bond or a linker atom or group,

t is zero or the integer 1,

u is an integer 1, 2 or 3,

Alk^3 is an aliphatic or heteroaliphatic chain and R^7 is a hydrogen or halogen atom or a group selected from alkyl, $-OR^8$, where R^8 is a hydrogen atom or an optionally substituted alkyl group, $-SR^8$, $-NR^8R^9$, where R^9 is as just defined for R^8 and may be the same or different, $-N[0]O_2$, -CN, $-C[0]O_2R^8$, $-SO_3H$, $-SOR^8$, $-SO_2R^8$ $-OC[0]O_2R^8$, $-CONR^8R^9$, $-OCONR^8R^9$, $-CSNR^8R^9$, $-COR^8$, $-OCOR^8$, $-N(R^8)COR^9$, $-N(R^8)CSR^9$, $-SO_2N(R^8)(R^9)$, $-N(R^8)SO_2R^9$, $-N(R^8)CON(R^9)(R^{10})$, where R^{10} is a

hydrogen atom or an optionally substituted alkyl group, $-N(R^8)CSN(R^9)(R^{IO})$ or $-N(R^8)SO_2N(R^9)(R^{10})$;

Alk^1 is an optionally substituted aliphatic or heteroaliphatic chain;

L^1 is a covalent bond or a linker atom or group;

Alk^2 is a straight or branched alkylene chain;

m is zero or an integer 1;

R^6 is a hydrogen atom or a methyl group;

r is zero or the integer 1;

R is a carboxylic acid (-C**[0]**$\underline{O}_2$H) or a derivative thereof;

R^a is a hydrogen atom or a methyl group;

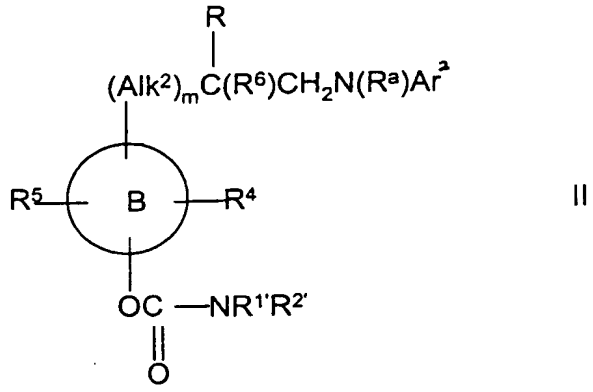
Ar^2 is an optionally substituted aromatic or heteroaromatic group;

B is a nitrogen containing heteroaryl group;

and the salts, solvates, hydrates and N-Oxides thereof.

Paragraph **[0014]** starting on Page 5:

Another class of compounds within the scope of this invention include compounds of formula **[(2)]**$\underline{\textbf{(II)}}$



II

Paragraph **[0015]** on Page 6:

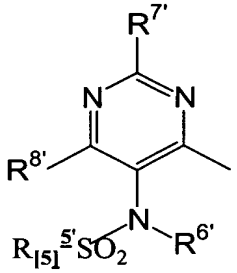
[0015] wherein R, R^a, R^4, R^5, R^6, Alk^2, B, *m* and Ar are as defined above and **[R^1 and R^2] $R^{1'}$ and $R^{2'}$** are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, aryl, cycloalkyl, substituted cycloalkyl, heterocyclic, heteroaryl or **[R^1 and R^2] $R^{1'}$ and $R^{2'}$**, together with the nitrogen atom to which they are attached, are joined to form an optionally substituted heterocyclic ring; and the salts, solvates, hydrates and N-oxides thereof.

Paragraph **[0016]** on Page 6:

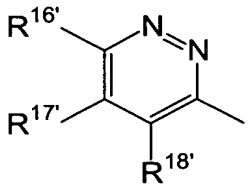
[0016] In one preferred embodiment, **[R^1 and R^2] $R^{1'}$ and $R^{2'}$** are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, cycloalkyl, substituted cycloalkyl, or **[R^1 and R^2] $R^{1'}$ and $R^{2'}$**, together with the nitrogen atom to which they are attached, are joined to form an optionally substituted heterocyclic ring provided that said substituted alkyl, substituted alkenyl and substituted cycloalkyl do not carry an aryl, substituted aryl, heteroaryl or substituted heteroaryl group.

Paragraph **[0017]** starting on Page 6:

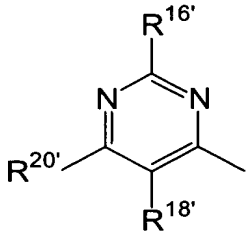
Preferably, in the compounds of this invention, Ar^2 is selected from the group consisting of moieties of formula IIIa, IIIc, IIId, IIIe or IIIf:



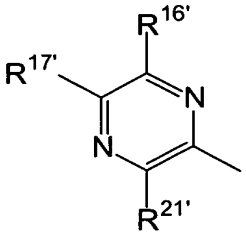
IIIa



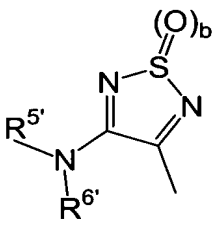
IIIc



IIId



IIIe



IIIf

Paragraph **[0027]** on Page 9:

[0027] It will be appreciated that compounds of formula (1) may have one or more chiral centers, and exist as enantiomers or diastereomers. The invention is to be understood to extend to all such enantiomers, diastereomers and mixtures thereof, including racemates. Formula (1) and **[(2)](II)** and the formulae hereinafter are intended to represent all individual isomers and mixtures thereof, unless stated or shown otherwise.

Paragraph **[0032]** starting on Page 10:

[0032] Particular examples of aliphatic chains represented by Alk^1 include optionally substituted $-CH_2-$, $-CH_2CH_2-$, $-CH(CH_3)-$, $-C(CH_3)_2-$, $-(CH_2)_2CH_2-$, $-CH(CH_3)CH_2-$, $-(CH_2)_3CH_2-$, $-CH(CH_3)CH_2CH_2-$, $-CH_2CH(CH_3)CH_2-$, $-C(CH_3)_2CH_2-$, $-(CH_2)_4CH_2-$, $-(CH_2)_5CH_2-$, $-CHCH-$, $-CHCHCH_2-$, $-CH_2CHCH-$, $-CHCHCH_2CH_2-$, $-CH_2CHCHCH_2-$, $-(CH_2)_2CHCH-$, $-CC-$, $-CCCH_2-$, $-CH_2CC-$, $-CCCH_2CH_2-$, $-CH_2CCCH_2-$, or $-(CH_2)_2CC-$ chains. Where appropriate each of said chains may be optionally interrupted by one or two atoms and/or groups L^4 to form an optionally substituted heteroaliphatic chain. Particular

examples include optionally substituted -L^4CH_2-, -C**H[h]**$_2L^4CH_2$-, -$L^4(CH_2)_2$-, -$CH_2L^4(CH_2)_2$-, $(CH_2)_2L^4CH_2$-, -$L^4(CH_2)_3$- and -$(CH_2)_2L^4(CH_2)_2$- chains. The optional substituents which may be present on aliphatic or heteroaliphatic chains represented by Alk^1 include one, two, three or more substituents where each substituent may be the same or different and is selected from halogen atoms, e.g. fluorine, chlorine, bromine or iodine atoms, or C_{1-6} alkoxy, e.g. methoxy or ethoxy, thiol, C_{1-6} alkylthio e.g. methylthio or ethylthio, amino or substituted amino groups. Substituted amino groups include -NHR^{12} and -$N(R^{12})_2$ groups where R^{12} is an optionally substituted straight or branched alkyl group as defined below for R^{11}. Where two R^{12} groups are present these may be the same or different. Particular examples of substituted chains represented by Alk^1 include those-specific chains just described substituted by one, two, or three halogen atoms such as fluorine atoms, for example chains of the type -$CH(CF_3)$-, -$C(CF_3)_2$- -$CH_2CH(CF_3)$-, -$CH_2C(CF_3)_2$-, -$CH(CF_3)$- and -$C(CF_3)_2CH_2$.

Paragraph **[0034]** starting on Page 11:

[0034] When in the compounds of formula (1) L^1, L^2 and/or L^3 is present as a linker atom or group it may be any divalent linking atom or group. Particular examples include -O- or -S- atoms or -C(O)-, -C(O)O-, -OC(O)-, -C(S)-, -S(O)-, -$S(O)_2$-, -$N(R^{II})$-, where R^{11} is a hydrogen atom or an optionally substituted alkyl group, -$CON(R^{11})$-, -$OC(O)N(R^{11})$-, -$CSN(R^{11})$-, -$N(R^{11})CO$-, -$N(R^{II})C(O)O$-, -$N(R^{11})CS$-, -$S(O)_2N(R^{11})$-, -$N(R^{II})S$**[0]**$O)_2$-, -$N(R^{11})$ $CON(R^{11})$-, -$N(R^{II})CSN(R^{II})$-, or -$N(R^{II})SO_2N(R^{II})$- groups. Where the linker group contains two R^{11} substituents, these may be the same or different.

Paragraph **[0042]** starting on Page 15:

[0042] Optional substituents which may be present on the aromatic or heteroaromatic groups represented by Ar^2 include one, two, three or more substituents, each selected from an atom or group R^{13} in which R^{13} is -R^{13a} or -Alk^4 (R^{13a})m,

wherein R^{13a} is a halogen atom, or an amino ($-NH_2$), substituted amino, nitro, cyano, amidino, hydroxyl (-OH), substituted hydroxyl, formyl, carboxyl (-C **[0]**O $_2$H), esterified carboxyl, thiol (-SH), substituted thiol, $-COR^{14}$, **[where R^{14} is an -$Alk^3(R^{13a})$m, aryl or heteroaryl group,]** $-CSR^{14}$, $-SO_3H$, $-SO_2R^{14}$ $-SO_2NH_2$, $-SO_2NHR^{14}$ $SO_2N(R^{14})_2$, $-CONH_2$, $-CSNH_2$, $-CONHR^{14}$, $-CSNHR^{14}$, $-CON(R^{14})_2$, $-CSN(R^{14})_2$, $-N(R^{12})SO_2R^{14}$, $-N(SO_2R^{14})_2$, $-NH^2(R^{11})SO_2NH_2$, $-N(R^{11})SO_2NHR^{14}$, $-N(R^{II})SO_2N(R^{14})_2$, $-N(R^{11})COR^{14}$, $-N(R^{11})CON(R^{14})_2$, $-N(R^{11})CSN(R^{14})_2$, $-N(R^{11})CSR^{14}$, $-N(R^{11})C(O)OR^{14}$, $-SO_2$ $NHet^1$, **[where -$NHet^1$ is an optionally substituted C_{5-7}cyclicamino group optionally containing one or more other -O- or -S- atoms or -$N(R^{11})$-, -C(O)- or -C(S)-groups,]** $-CONHet^1$, $-CSNHet^1$, $-N(R^{11})SO_2NHet^1$, $-N(R^{11})CONHet^1$,$-N(R^{II})CSNHet^1$, $-Het^2$, **[where Het^2 is an optionally substituted monocyclic C_{5-7}carbocyclic group optionally containing one or more -O- or -S- ,atoms or -$N(R^{II})$-,-C(O)- or -C(S)- groups,]** $-SO_2N(R^{II})Het^2$, $-CON(R^{11})Het^2$, $-CSN(R^{II})Het^2$, $-N(R^{11})CON(R^{11})Het^2$, $-N(R^{II})CSN(R^{II})Het^2$, aryl or heteroaryl group;

wherein

R^{14} is aryl or heteroaryl group,

-$NHet^1$ is an optionally substituted C_{5-7}cyclicamino group optionally containing one or more other -O- or -S- atoms or -$N(R^{11})$-, -C(O)- or -C(S)-groups,

Het^2 is an optionally substituted monocyclic C_{5-7}carbocyclic group optionally containing one or more -O- or -S- ,atoms or -$N(R^{II})$-, -C(O)- or -C(S)-groups,

Alk^4 is a straight or branched C_{1-6}alkylene, C_{2-6}alkenylene or C_{2-6}alkynylene chain, optionally interrupted by one, two or three -O- or -S- atoms or $-S(O)_n$, where n is an integer 1 or 2, or $-N(R^{15})$- groups, where R^{15} is a hydrogen atom or C_{1-6}alkyl, e.g. methyl or ethyl group; and m is zero or an integer 1, 2 or 3. It will be appreciated that when two R^{11} or R^{14} groups are present in one of the above substituents, the R^{11} or R^{14} groups may be the same or different.

Paragraph **[0047]** starting on Page 16:

[0047] Esterified carboxyl groups represented by the group R^{13a} include groups of formula -C **[0]**O $_2Alk^5$ wherein Alk^5 is a straight or branched, optionally substituted C_{1-8}alkyl group such as a methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl or t-butyl group; a $C_{6-12}arylC_{1-8}$alkyl group such as an optionally substituted benzyl, phenylethyl, phenylpropyl, 1-naphthylmethyl or 2-naphthylmethyl group; a C_{6-12}aryl group such as an optionally substituted phenyl, 1-naphthyl or 2-naphthyl group; a $C_{6-12}aryloxyC_{1-8}$ alkyl group such as an optionally substituted phenyloxymethyl, phenyloxyethyl,1-naphthyl-oxymethyl, or 2-naphthyloxymethyl group; an optionally substituted $C_{1-8}alkanoyloxyC_{1-8}$alkyl group, such as a pivaloyloxymethyl, propionyloxyethyl or propionyloxypropyl group; or a $C_{6-12}aroyloxyC_{1-8}$alkyl group such as an optionally substituted benzoyloxyethyl or benzoyloxypropyl group. Optional substituents present on the Alk^5 group include R^{13a} substituents described above.

Paragraph **[0051]** starting on Page 18:

[0051] Particularly useful atoms or groups **which can be substituents on Ar^2 [represented by R^{13}]** include fluorine, chlorine, bromine or iodine atoms, or C_{1-6}alkyl, e.g. methyl, ethyl, n-propyl, i-propyl, n-butyl or t-butyl, optionally substituted phenyl, pyridyl, pyrimidinyl,pyrrolyl, furyl, thiazolyl, or thienyl, morpholinyl, thiomorpholinyl, piperazinyl,pyrrolidinyl, piperidinyl, C_{1-6}alkylamino, e.g. methylamino or ethylamino, C_{1-6}hydroxyalkyl, e.g. hydroxymethyl or hydroxyethyl, $carboxyC_{1-6}$alkyl, e.g. carboxyethyl, C_{1-6}alkylthio e.g. methylthio or ethylthio, $carboxyC_{1-6}$alkylthio, e.g. carboxymethylthio, 2-carboxyethylthio or 3-carboxy-propylthio, C_{1-6}alkoxy, e.g. methoxy or ethoxy, $hydroxyC_{1-6}$alkoxy, e.g. 2-hydroxyethoxy, optionally substituted phenoxy, pyridyloxy, thiazolyoxy,phenylthio or pyridylthio, C_{5-7}cycloalkoxy, e.g. cyclopentyloxy, $haloC_{1-6}$alkyl, e.g. trifluoromethyl, $haloC_{1-6}$alkoxy, e.g. trifluoromethoxy, C_{1-6}alkylamino, e.g. methylamino or ethylamino or propylamino, optionally substituted $C_{6-12}arylC_{1-6}$alkylamino,

e.g. benzylamino, fluorobenzylamino or hydroxyphenylethylamino, amino ($-NH_2$), amino C_{1-6}alkyl, e.g.aminomethyl or aminoethyl, C_{1-6}dialkylamino, e.g. dimethylamino or diethylamino, aminoC_{1-6}alklamino e.g. aminomethylamino, aminoethylamino or aminopropylamino, Het^{1}NC_{1-6}alkylamino e.g. morpholinopropylamino, C_{1-6}alkylaminoC_{1-6}alkyl, e.g. ethylaminoethyl, C_{1-6}dialkylaminoC_{1-6}alkyl, e.g. diethylaminoethyl, aminoC_{1-6}alkoxy, e.g. aminoethoxy, C_{1-6}alkylaminoC_{1-6}alkoxy, e.g. methylaminoethoxy, C_{1-6}dialkylaminoC_{1-6}alkoxy, e.g. dimethylaminoethoxy, diethylaminoethoxy, diisopropylaminoethoxy, or dimethylaminopropoxy, hydroxyC_{1-6}alkylamino,e.g. hydroxyethylamino, hydroxypropylamino or hydroxybutyfamino, imido, such as phthalimido or naphthalimido, e.g. 1,8-naphthalimido, vitro, cyano, amidino, hydroxyl (-OH), formyl [HC(O)-], carboxyl ($-CO_2H$), $-CO_2Alk^5$, where Alk^5 is as defined above, C_{1-6}alkanoyl e.g. acetyl, propyryl or butyryl, optionally substituted benzoyl, thiol (-SH), thioC_{1-6}alkyl, e.g. Thiomethyl or thioethyl, $-SC(=NH)NH_2$, sulphonyl ($-SO_3H$), C_{1-6}alkyl-sulphinyl, e.g. methylsulphinyl, ethylsulphinyl or propylsulphinyl, C_{1-6}alkylsulphonyl, e.g. methylsulphonyl, ethylsulphonyl, propylsulphonyl, hexylsulphonyl or isobutylsulphonyl, aminosulphonyl ($-SO_2NH_2$), C_{1-6}alkylaminosulphonyl, e.g. methylaminosulphonyl, ethylaminosulphonyl or propylaminocsulphonyl, C_{1-6}dialkylaminosulphonyl, e.g. dimethylamino-sulphonyl or diethylaminosulphonyl, optionally substituted phenylamino-sulphonyl, carboxamido ($-CONH_2$), C_{1-6}alkylaminocarbonyl, e.g. methylaminocarbonyl, ethylaminocarbonyl or propylaminocarbonyl, C_{1-6}dialkylaminocarbonyl, e.g. dimethylaminocarbonyl, diethylaminocarbonyl or dipropylaminocarbonyl, aminoC_{1-6}alkylaminocarbonyl, e.g. Aminoethylaminocarbonyl, C_{1-6} dialkylaminoC_{1-6}alkylaminocarbonyl, e.g. diethylaminoethylaminocarbonyl, aminocarbonylamino, C_{1-6}alkylaminocarbonyl-amino, e.g. methylaminocarbonylamino or ethylaminocarbonylamino, C_{1-6}dialkylaminocarbonylamino, e.g. dimethylaminocarbonylamino or diethylaminocarbonylamino, C_{1-6}alkylaminocabonylC_{1-6}alkylamino, e.g. methylaminocarbonylmethylamino, aminothiocarbonylamino,

C_{1-6}alkyl-aminothiocarbonylamino, e.g. methylaminothiocarbonylamino or ethylaminothiocarbonylamino, C_{1-6} dialkylaminothiocarbonylamino, e.g. dimethylaminothiocarbonylamino or diethylaminothiocarbonylamino, C_{1-6}alkylaminothiocarbonylC_{1-6}alkylamino, e.g. ethylaminothiocarbonylmethylamino, -CONHC(=NH)NH_2, C_{1-6}alkylsulphonylamino, e.g. methylsulphonylamino or ethylsulphonylamino, C_{1-6}dialkylsulphonylamino, e.g. dimethylsulphonylamino or diethylsulphonylamino, optionally substituted phenylsulphonylamino, aminosulphonylamino (-$NHSO_2NH_2$), C_{1-6}alkylaminosulphonylamino, e.g. methylaminosulphonylamino or ethylaminosulphonylamino, C_{1-6}dialkylaminosulphonylamino, e.g. dimethylaminosulphonyl-amino or diethylaminosulphonylamino, optionally substituted morpholine-sulphonylamino or morpholinesulphonylC_{1-6}alkyl-amino, optionally substituted phenylaminosulphonylamino, C_{1-6}alkanoylamino, e.g. Acetylamino, aminoC_{1-6}alkanoylamino e.g. Aminoacetylamino, C_{1-6}dialkylaminoC_{1-6}alkanoylamino, e.g. dimethylaminoacetylamino, C_{1-6} alkanoylaminoC_{1-6}alkyl, e.g. Acetylaminomethyl, C_{1-6}alkanoylaminoC_{1-6} alkylamino, e.g. Acetamidoethylamino, C_{1-6}alkoxycarbonylamino, e.g. methoxycarbonylamino, ethoxycarbonylamino or t-butoxycarbonylamino or optionally substituted benzyloxy, pyridylmethoxy, thiazolylmethoxy, benzyloxycarbonylamino, benzyloxycarbonylaminoC_{1-6}- alkyl e.g. benzyloxy carbonylaminoethyl, thiobenzyl, pyridylmethylthio or thiazolylmethylthio groups.

Delete paragraph **[0058]** starting on Page 21:

[0058] [One particular class of compounds of formula (1) is that wherein g is zero.]

Paragraph **[0067]** starting on Page 23:

[0067] In compounds of formulae (1) and (2) m is preferably 1 and Alk^2 is preferably -CH_2-**[; g in these compounds is preferaly zero]**.

Paragraph **[0072]** starting on Page 24:

[0072] [Particularly useful R^{13}] **Other atoms or groups which can be** substituents **[of these types]** **on Ar^2** include a halogen atom, especially fluorine or chlorine, morpholinyl, thiomorpholinyl, optionally substituted piperidinyl, especially piperidinyl or 4-carboxypiperidinyl, pyrrolidinyl, optionally substituted piperazinyl, especially t-butyloxycarbonylpiperazinyl, thioC_{1-6}alkyl, especially thiomethyl, thioethyl or thiopropyl, optionally substituted thiobenzyl, especially thiobenzyl, haloC_{1-6}alkyl, especially trifluoromethyl, C_{1-6}alkyloxy, especially methoxy, ethoxy or propoxy, optionally substituted benzyloxy, especially benzyloxy, haloC_{1-6}alkoxy, especially trifluoromethoxy and difluoromethoxy, C_{1-6}alkylamino, especially methylamino, ethylamino or propylamino, C_{1-6}dialkylamino, especially dimethylamino or diethylamino, optionally substituted C_{6-12}arylC_{1-6}alkylamino, especially benzylamino, 4-substituted benzyl, especially 4-fluorobenzylamino or 4-hydroxyphenylethylamino, aminoalkylamino, especially 3-aminopropylamino, Het^1 NC_{1-6}alkylamino, especially 3-morpholinopropylamino, optionally substituted phenoxy, especially phenoxy, hydroxyC_{1-6}alkylamino, especially 2-hydroxyethylamino, 3-hydroxypropylamino and 3-hydroxybutylamino, nitro, carboxyl, $-CO_2Alk^5$, where R^5 is as defined above, especially carboxymethyl and carboxyethyl, carboxamido, C_{1-6}alkylaminocarbonyl, especially methylaminocarbonyl, ethylaminocarbonyl and propylaminocarbonyl, C_{1-6}dialkylaminocarbonyl, especially dimethylaminocarbonyl, diethylaminocarbonyl or dipropylaminocarbonyl, C_{1-6}alkanoyl, especially acetyl, propyryl or butyryl, optionally substituted benzoyl, especially benzoyl, C_{1-6} alkylsulphinyl, especially methylsulphinyl, ethylsulphinyl or propylsulphinyl, C_{1-6}alkylsulphonyl, especially methylsulphonyl, ethylsulphonyl, propylsulphonyl, hexylsulphonyl or isobutylsulphonyl, C_{1-6}alkylaminosulphonyl, especially ethylaminosulfonyl or propylaminosulphonyl, C_{1-6}dialkylaminosulphonyl, especially diethylaminosulphonyl, C_{1-6}alkylaminocarbonyl, especially methylaminocarbonyl, ethylaminocarbonyl or propylaminocarbonyl, C_{1-6}dialkylaminocarbonyl, especially dimethylaminocarbonyl or diethylaminocarbonyl.

Paragraph **[0159]** starting on Page 56:

[0159] In a further example compounds of formula (4) [R^a, R^6 are H**[, g is zero]**] can be converted into compounds of formula (5) by treatment with nitrous acid, or isoamyl nitrite in the presence of an acid source, for example acetic acid, in a halogenated hydrocarbon e.g. dichloromethane or chloroform at a temperature from ambient temperature to 60°C.

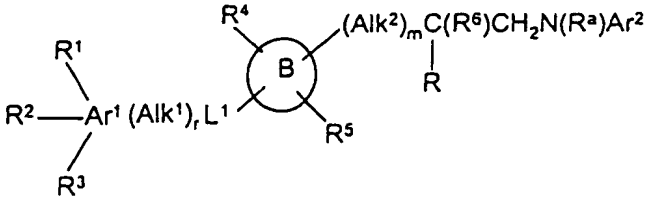
Paragraph **[0167]** starting on Page 59:

[0167] In a further example compounds may be obtained by sulphonylation of a compound containing an -OH group by reaction with one of the above alkylating agents but in which **[X2]**$\underline{X^2}$ is replaced by a -S(O)Hal or -SO_2Hal group, in which Hal is a halogen atom such as chlorine atom**[]**, in the presence of a base, for example an inorganic base such as sodium hydride in a solvent such as an amide, e.g. a substituted amide such as dimethylformamide at for example ambient temperature.

In the Claims

3. (Amended) The compound according to Claim 2 wherein $R^{1'}$ and $R^{2'}$ are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, cycloalkyl, substituted cycloalkyl, or **[R^1 and R^2]** $\underline{R^{1'}$ and $R^{2'}}$, together with the nitrogen atom to which they are attached, are joined to form an optionally substituted heterocyclic ring provided that said substituted alkyl, substituted alkenyl and substituted cycloalkyl do not carry an aryl, substituted aryl, heteroaryl or substituted heteroaryl group.

4. (Amended) A compound of the formula:



(1)

wherein

Ar^1 is an aromatic or heteroaromatic group;

R^1, R^2, R^3, R^4 and R^S which may be the same or different is each an atom or group $-L^2(Alk^3)_tL^3(R^7)_u$ in which L^2 and L^3 which may be the same or different is each a covalent bond or a linker atom or group, t is zero or the integer 1, u is an integer 1, 2 or 3, Alk^3 is an aliphatic or heteroaliphatic chain and R^7 is a hydrogen or halogen atom or a group selected from alkyl, $-OR^8$, where R^8 is a hydrogen atom or an optionally substituted alkyl group, $-SR^8$, $-NR^8R^9$, where R^9 is as just defined for R^8 and may be the same or different, $-NO_2$, -CN, $-CO_2R^8$, $-SO_3H$, $-SOR^8$, $-SO_2R^8$, $-OCO_2R^8$, $-CONR^8R^9$, $-OCONR^8R^9$, $-CSNR^8R^9$, $-COR^8$, $-OCOR^8$, $-N(R^8)COR^9$, $-N(R^8)CSR^9$, $-SO_2N(R^8)(R^9)$, $-N(R^8)SO_2R^9$, $-N(R^8)CON(R^9)(R^{10})$, where R^{10} is a hydrogen atom or an optionally substituted alkyl group, $-N(R^8)CSN(R^9)(R^{10})$ or $-N(R^8)SO_2N(R^9)(R^{10})$;

Alk^1 is an optionally substituted aliphatic or heteroaliphatic chain;

L^1 is a covalent bond or a linker atom or group;

Alk^2 is a straight or branched alkylene chain;

m is zero or an integer 1;

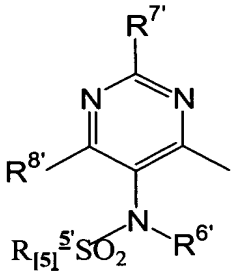
R^6 is a hydrogen atom or a methyl group;

r is zero or the integer 1;

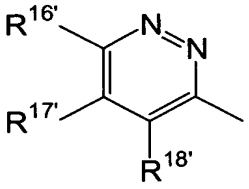
R is a carboxylic acid ($-CO_2H$) or a derivative thereof;

R^a is a hydrogen atom or a methyl group;

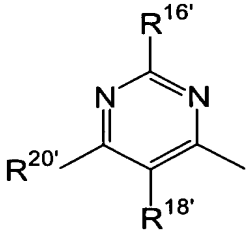
Ar^2 is selected from the group consisting of moieties of formula IIIa, IIIc, IIId, IIIe and IIIf:



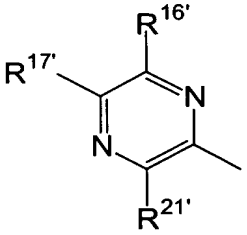
IIIa



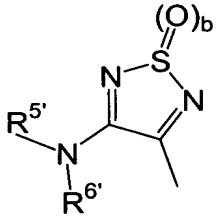
IIIc



IIId



IIIe



IIIf

where $R^{5'}$ is selected from the group consisting of alkyl, substituted alkyl, alkenyl, substituted alkenyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocylic, heteroaryl'and substituted heteroaryl;

$R^{6'}$ is selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, and $-SO_2R^{10'}$ where $R^{10'}$ is selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl;

$R^{7'}$ and $R^{8'}$ are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen;

$R^{16'}$ and $R^{17'}$ are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen; and

$R^{18'}$ is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

$R^{20'}$ is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen;

$R^{21'}$ is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heterocyclic and substituted heterocyclic;

b is 1 or 2;

B is a nitrogen containing heteroaryl group;

and enantiomers, diastereomers and pharmaceutically acceptable salts thereof.